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Objectives

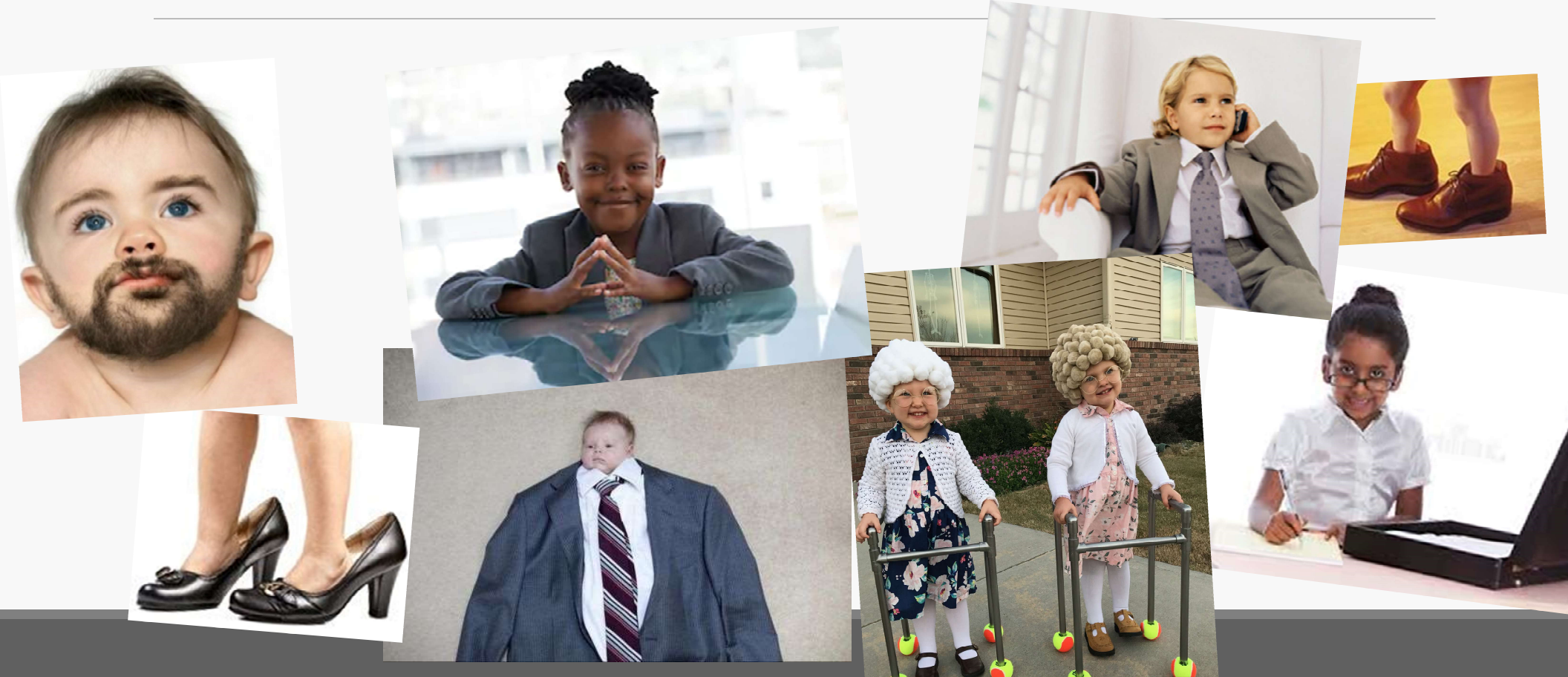
Review why children are more vulnerable to TB

Understand how the epidemiology of TB differs in children

Describe approaches to TB testing in children: IGRAs vs TST

Understand how LTBI regimens can be catered to children

Children are not little adults



How TB differs among children

- Usually primary disease rather than reactivation
- Non-specific findings
- Invasive nature of obtaining a quality specimen
- Disease is paucibacillary in most children
- Challenges with treatment administration

Risk varies by age

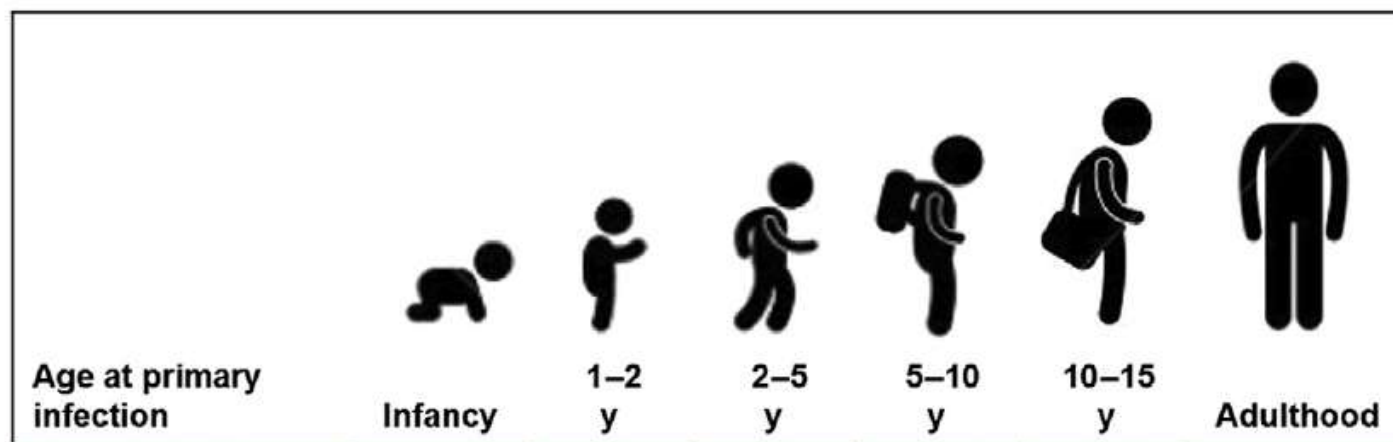



Fig. 2. Age-related risks of TB disease after primary infection in the prechemotherapy era.^a Lifetime risk. (Adapted from Marais BJ, Gie RP, Schaaf HS, et al. The clinical epidemiology of childhood pulmonary tuberculosis: a critical review of literature from the pre-chemotherapy era. *Int J Tuberc Lung Dis* 2004;8(3):278–85.)

Risk varies by age




Age at primary infection	Infancy	1–2 y	2–5 y	5–10 y	10–15 y	Adulthood
Risk of pulmonary disease (%)	30–40	10–20	5	2	10–20	5–10 ^a
Risk of disseminated disease (%)	10–20	2–5	0.5	<0.5	<0.5	<0.5

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A sentinel event:

Represents recent (3-12 mos) community transmission



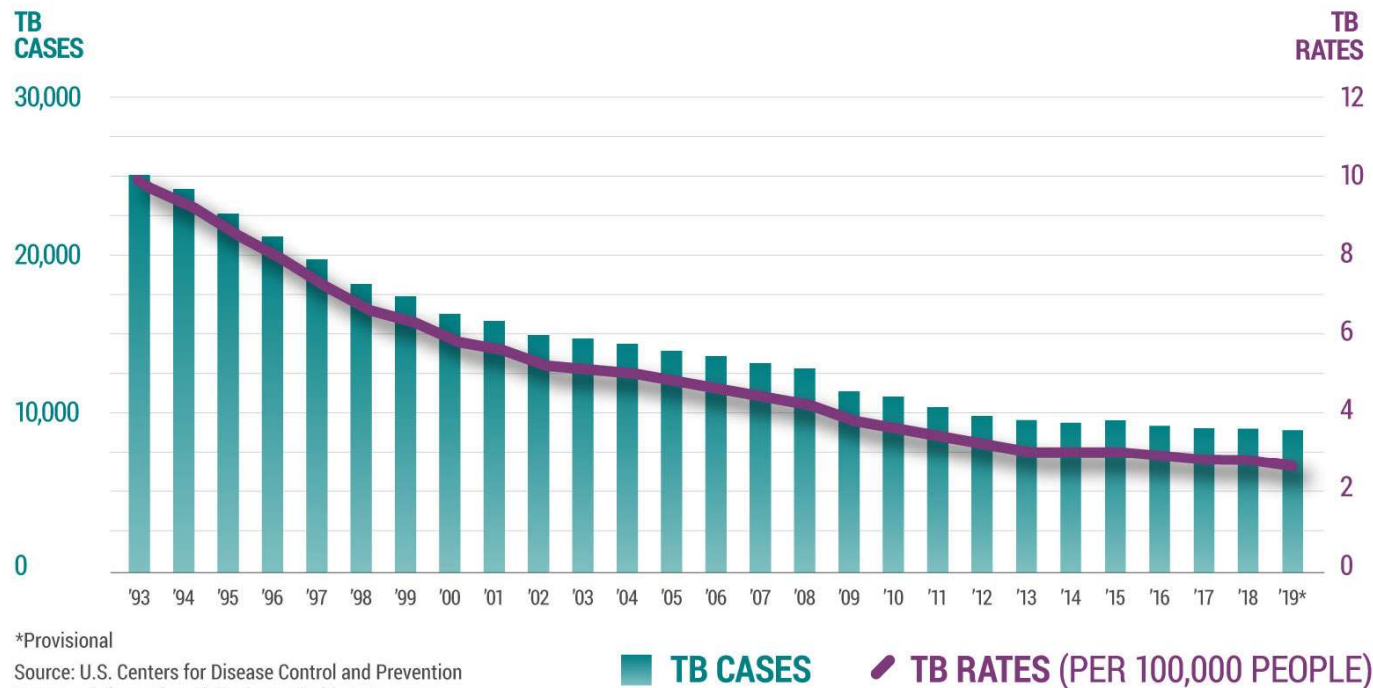
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Epidemiology of Childhood TB

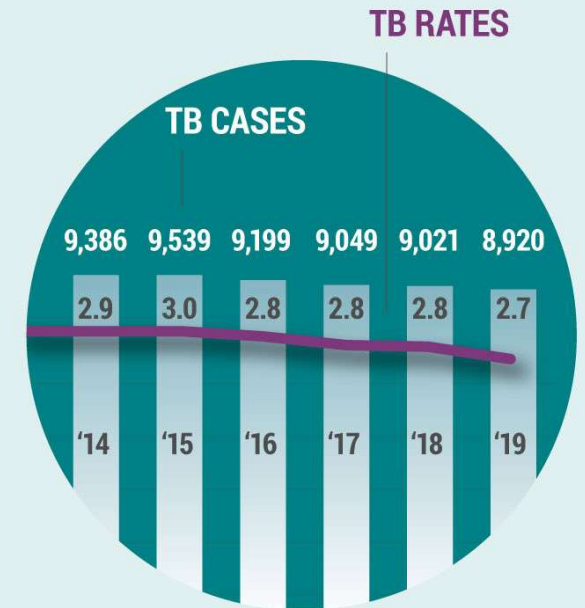
The path to TB elimination is clear, **but progress has slowed in recent years**

REPORTED TB CASES and TB RATES in the U.S., 1993–2019*



*Provisional

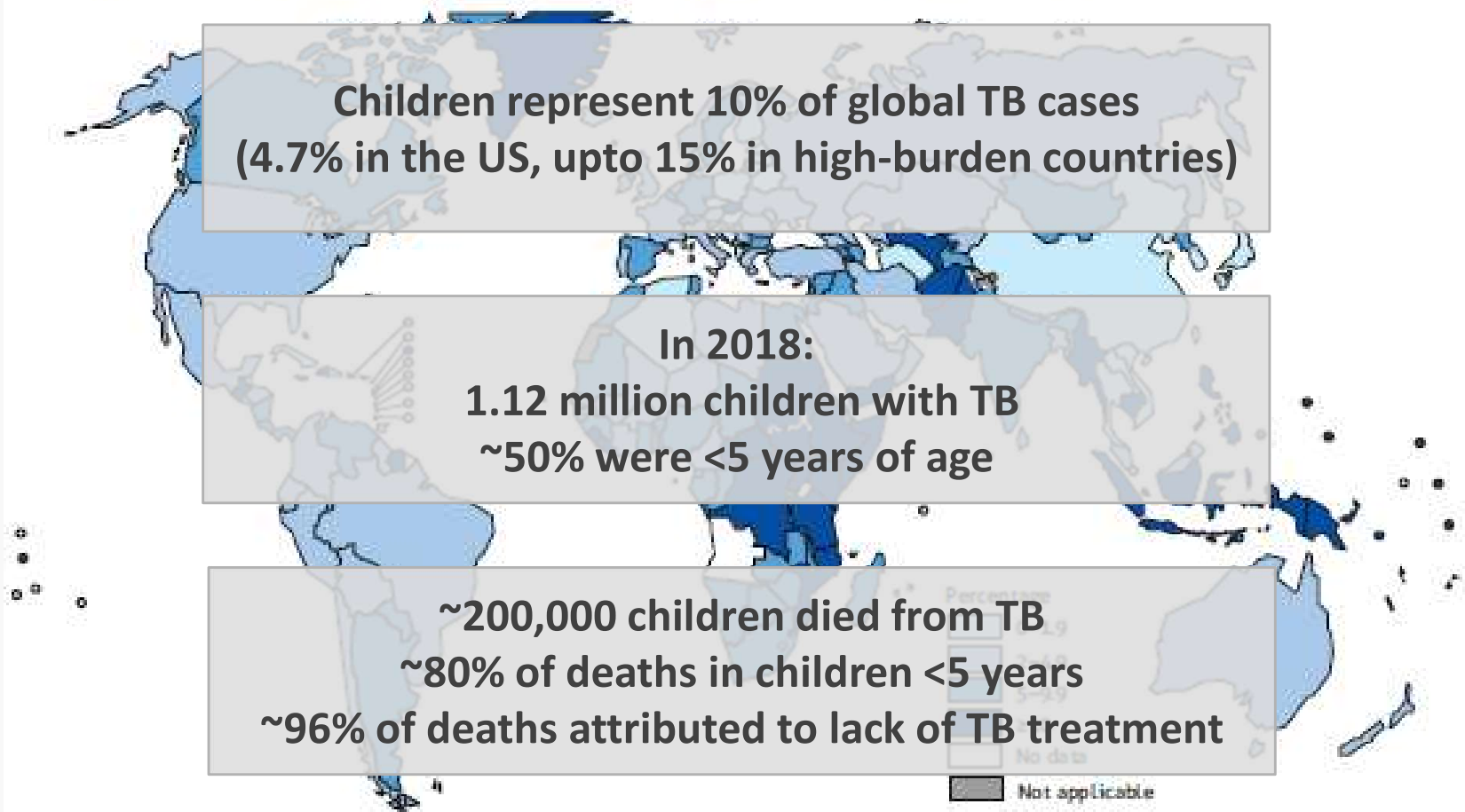
Source: U.S. Centers for Disease Control and Prevention
For more information, visit [cdc.gov/nchhstp/newsroom](https://www.cdc.gov/nchhstp/newsroom)



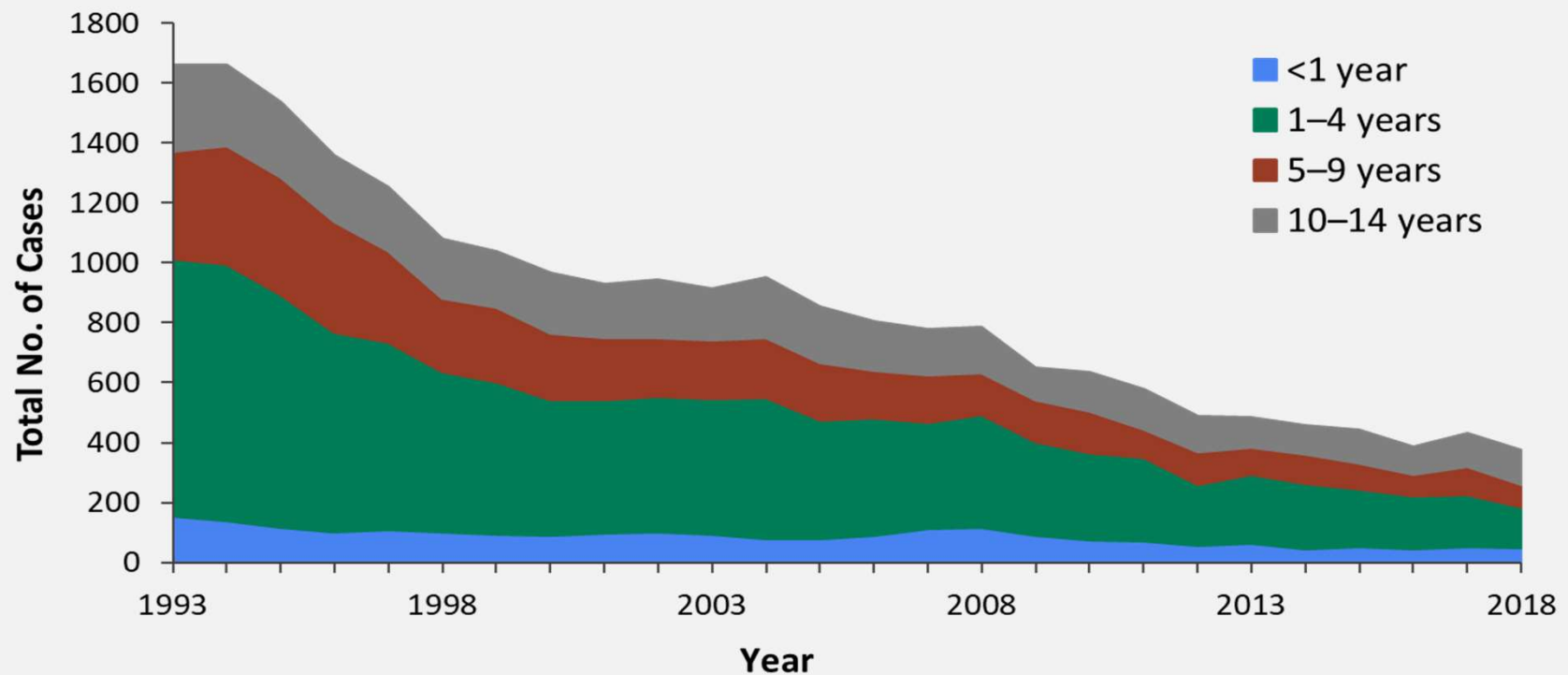
It's time to
**ELIMINATE
TUBERCULOSIS
IN THE U.S.**

FIG. 4.4

Percentage of new and relapse TB cases that were children (aged <15), 2018

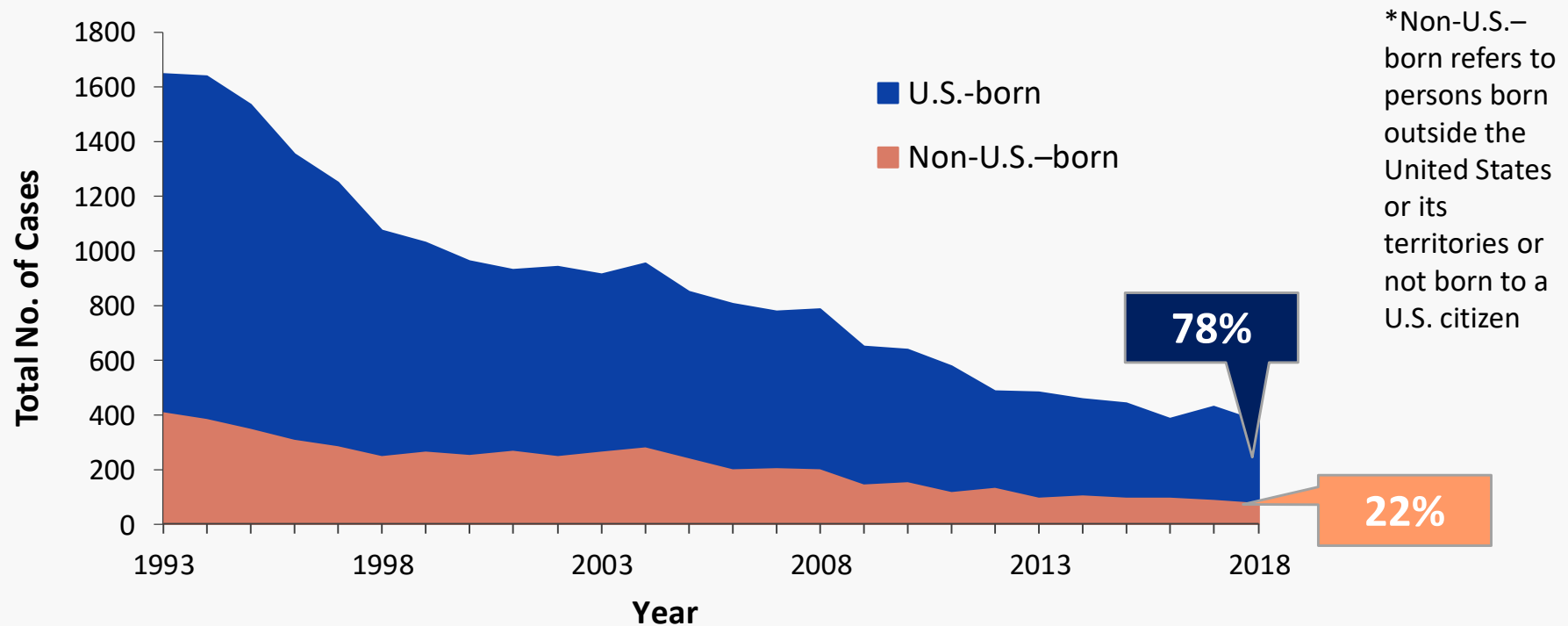


Pediatric TB Cases by Age Group, 1993–2018

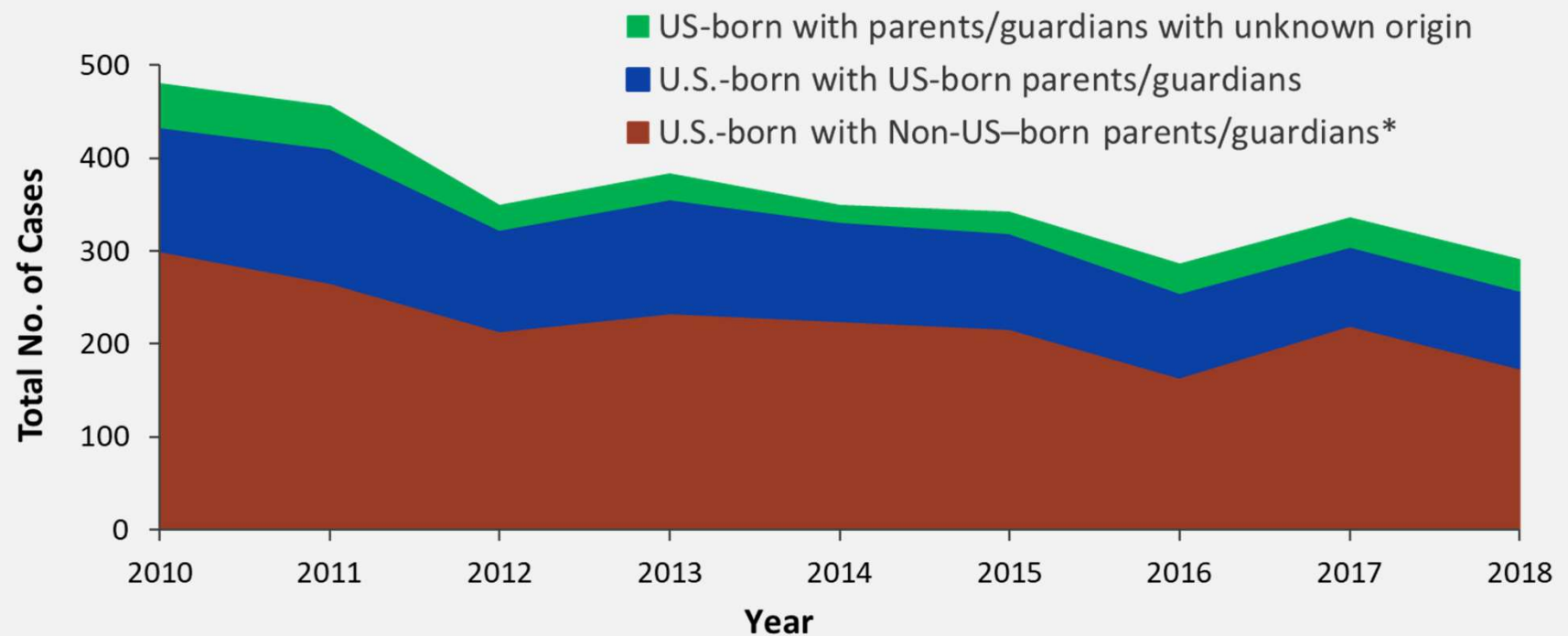


Pediatric TB is more common in US-born

Number of U.S. Pediatric TB Cases among U.S.-Born and Non-U.S.-Born* Children, 1993–2018

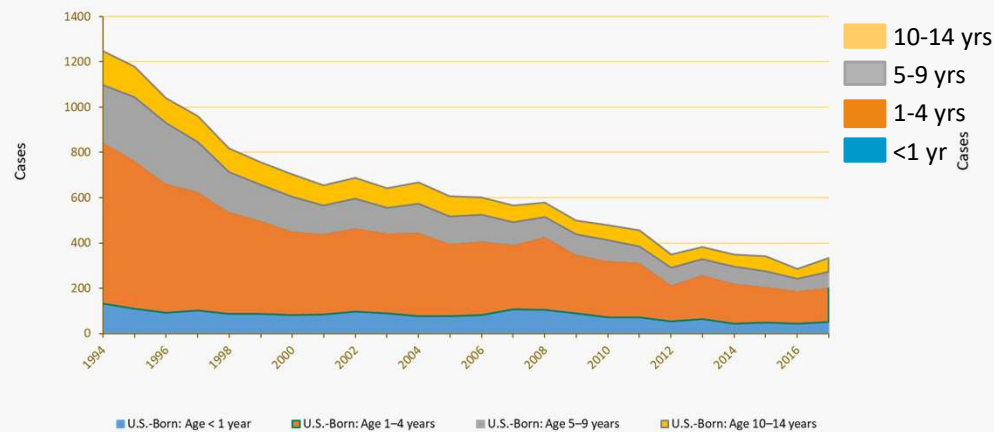


Number of U.S. Pediatric TB Cases among U.S.-Born Children by Parent Status, 2010–2018

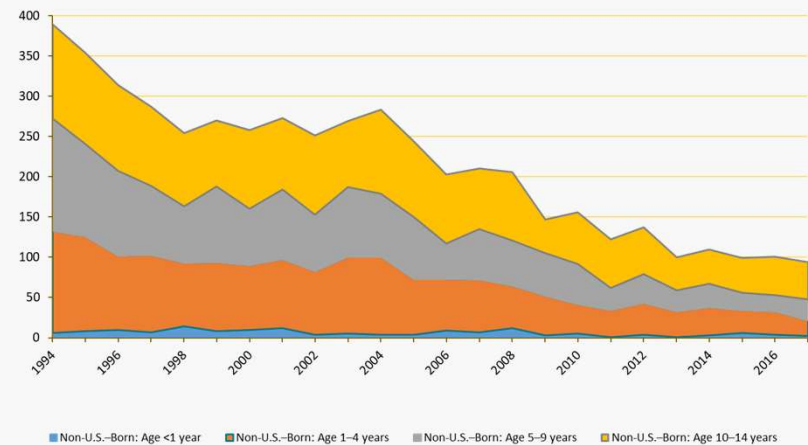


Pediatric TB Cases by Age Group, 1994–2017

U.S.-BORN CHILDREN, N=15,186



NON-U.S.-BORN* CHILDREN, N=5,131



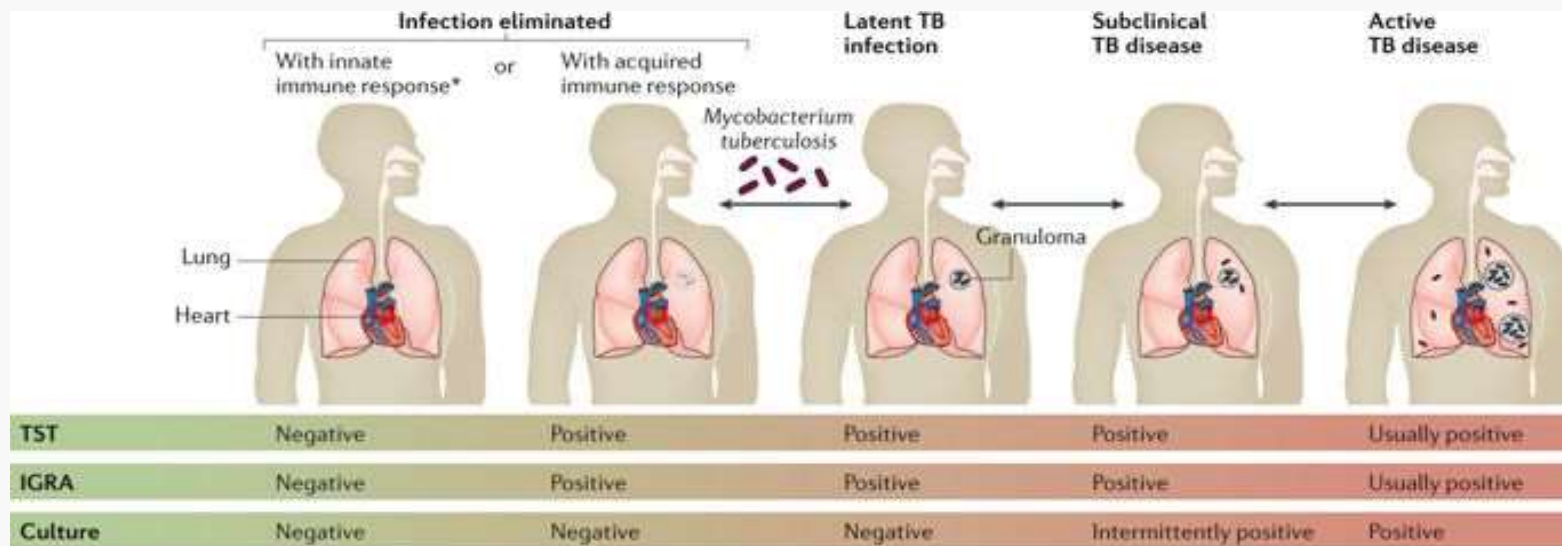
*Non-U.S.-born refers to persons born outside the United States or its territories or not born to a U.S. citizen



to use IGRAs in
young children

Testing Strategies

Tuberculosis infection



Which test to use: TST vs IGRA?

TABLE 1 Comparison of the TST and IGRAs

Characteristic	TST	IGRA
Estimated specificity in BCG-unvaccinated children	95% to 100%	90% to 95%
Estimated specificity in BCG-vaccinated children	49% to 65%	89% to 100%
Estimated sensitivity (confirmed TB disease)	75% to 85%	80% to 85%
Estimated sensitivity (clinical TB disease)	50% to 70%	60% to 80%

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FIG 3.11. GUIDANCE ON STRATEGY FOR USE OF TST AND IGRA FOR DIAGNOSIS OF LTBI BY AGE AND BCG

AAP guidance from 2018 Red Book:

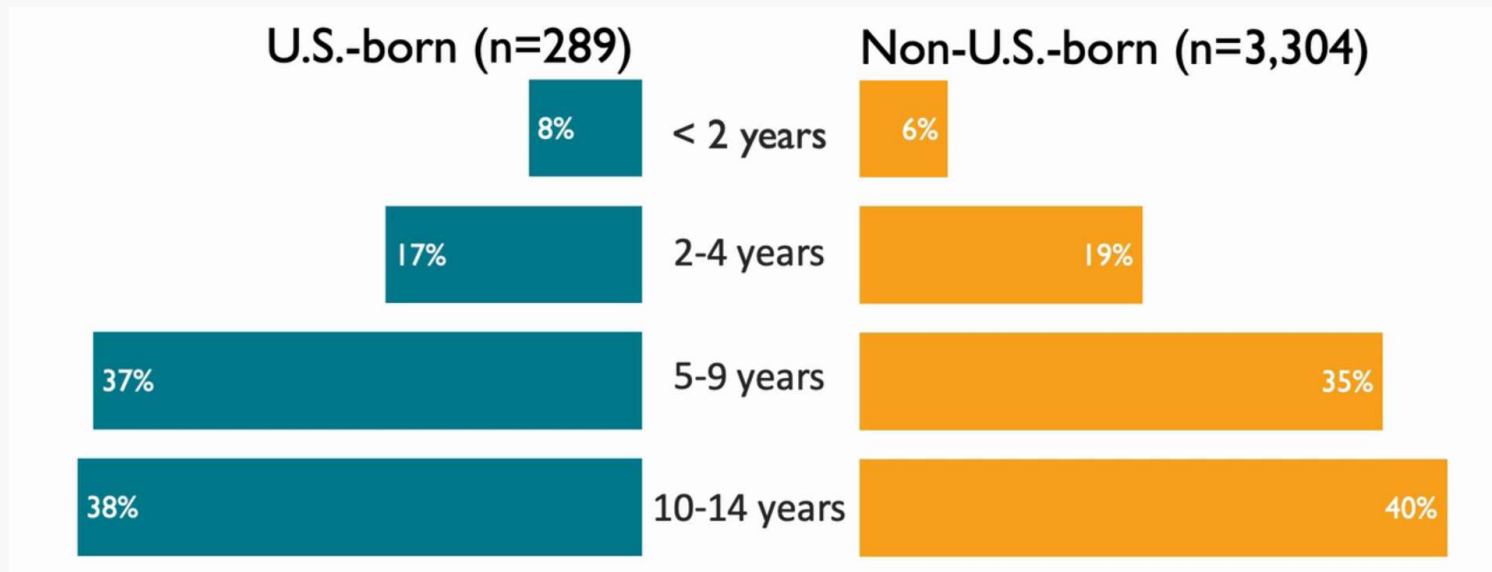
- Use a targeted approach to testing children at high risk.
- Can use IGRAs in any child ≥ 2 years of age (and especially those with BCG vaccination)
- Preference for using TST in children <2 years of age

Infants/Toddlers <2 years exposed to TB:

- If TST is negative, check an IGRA to maximize sensitivity (and if IGRA positive, act on those results)

Interferon- γ Release Assays in Children <15 Years of Age

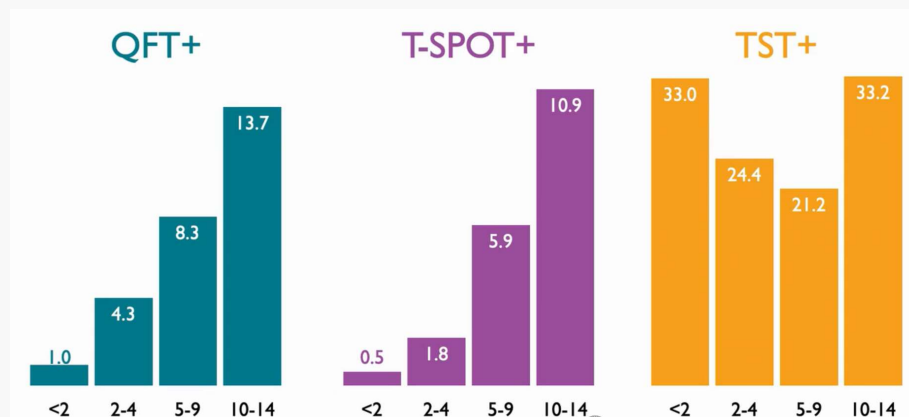
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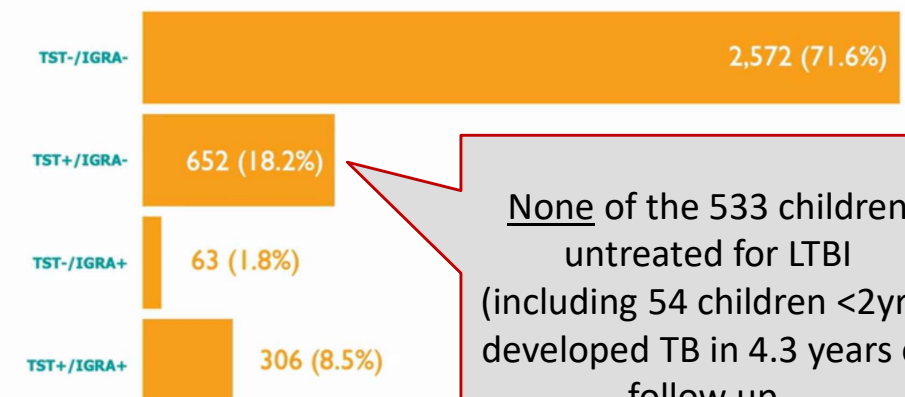
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SINGLE TEST POSITIVITY (NON-US BORN) BY AGE



FREQUENCY OF COMBINATION RESULTS (N=3,595)



None of the 533 children untreated for LTBI (including 54 children <2yrs) developed TB in 4.3 years of follow up.



The Case for Retiring the Tuberculin Skin Test

Andrea T. Cruz, MD, MPH,^a Lee B. Reichman, MD, MPH^b

To TST or not to TST, that is the question! Part 1: TB Infection

by Ana M. Alvarez MD, University of Florida College of Medicine, Jacksonville, FL, Wolfson Children's Hospital, Jacksonville, FL ;

Lower sensitivity in certain conditions:

- Age <3-6 months.
- Immunosuppression (steroids, chemo, etc)
- Immunocompromising conditions (HIV, malnutrition, malignancy, active TB itself)

Lower specificity:

- NTM infection
- Recent BCG vaccination

Issues with the assay (storage):

- Light sensitivity
- Adsorption to plastic

Administration/Interpretation issues: quality control?

Cost?

Transparency of results?

Familiarity?



to use short-course
LTBI regimens

Treatment
Strategies:
LTBI and TB exposure

Guidelines for the Treatment of Latent Tuberculosis Infection: Recommendations from the National Tuberculosis Controllers Association and CDC, 2020

Drug(s)	Duration	Abbrev	Notes
Isoniazid+ Rifapentine (+B6)	Weekly for 3 months	3HP	Weekly administration, DOT or SAT Not approved for <2yrs
Rifampin	Daily for 4 months	4R	Can be used in all ages, caution about drug-drug interactions.
Isoniazid + Rifampin	Daily for 3 months	3HR	“Preferred” by CDC, “Alternative regimen” by AAP/2018 Red Book. Caution about drug-drug interactions.
Isoniazid (+B6)	6 months 9 months	6H 9H	“Alternative regimen” by CDC Daily SAT or twice-weekly administration via DOT

Care of infants and toddlers exposed to TB



Window prophylaxis for infants and children <5 yrs exposed to TB

Isoniazid 10-20 mg/kg/daily for 8-10 weeks, pending reassessment

- Isoniazid 20-30 mg/kg/dose **twice weekly**:
 - Equivalent efficacy compared to daily administration.

Neonates/infants in whom TST is deemed too unreliable:

- Isoniazid 20-30 mg/kg/dose **twice weekly** for 6 months (presumed LTBI)
- Consideration of daily 4R (presumed LTBI)



to advocate for
child-friendly
dosing



Adolescents with TB

Age 10-19 years

Rise in incidence of LTBI and TB disease

- Hormonal influence? Immunologic factors? Changes in social patterns?

Challenges with medication adherence, loss to follow up, stigma

Teen-friendly services may improve success:

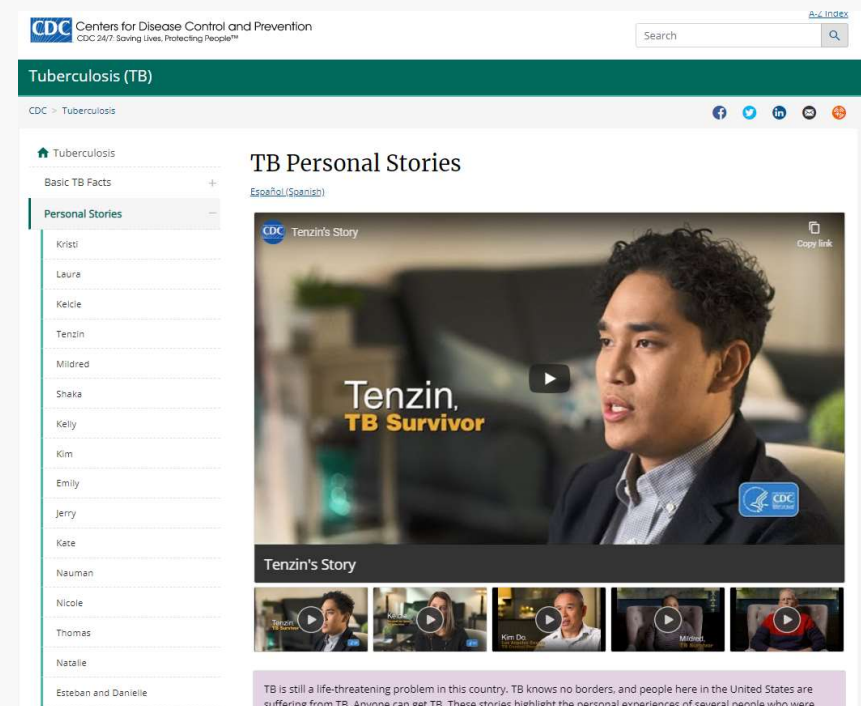
- Extended hours for clinic visits
- Computer based interventions, text messaging to improve adherence and retention
- Behavioral interventions to assess depression, stigma, substance abuse counseling
- Peer support groups

Supporting children & families

Informational handouts for parents: window prophylaxis

TB personal stories:

- <https://www.cdc.gov/tb/topic/basics/personalstories.htm>
- Toddlers (Rick and Francene)
- Children (Rosalie and Faith)
- High schoolers (Sarah)
- College (Tri)



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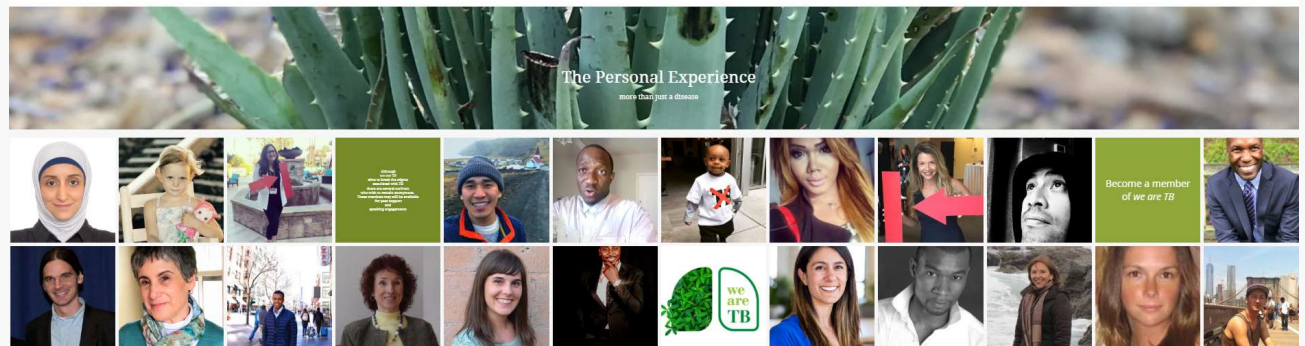
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We are TB:

- <https://www.wearetb.com/>
- Support groups



Summary

- Infancy and adolescence represent vulnerable periods in TB progression and management.
- Testing for TB should be limited to at-risk populations
 - IGRAs can be used in children ≥ 2 years of age,
 - evidence is mounting for children <2 years
- We have several shorter LTBI regimens that can make treatment more feasible for children and families
- We can tailor our support for children and adolescents to maximize success of TB treatments.

IT'S TIME to
build capacity

IT'S TIME to speak up

IT'S TIME to
end stigma

IT'S TIME to test and
treat latent TB infection

**IT'S
TIME → END
TB**

A world map is centered on a wooden-textured background. The map is dark brown, and the continents are cut out, revealing the wood grain. Numerous small blue dots are scattered across the map, primarily concentrated in Africa, Asia, and South America, representing TB prevalence. A red circular arrow with a dashed line inside it encircles the Americas. A red arrow points from the word 'TIME' to the words 'END TB'.